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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,536	03/28/2001	Preeti Lal	PF-0610 USN	1220

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Incyte Genomics Inc
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EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	PAPER NUMBER
1646	11

DATE MAILED: 09/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/806,536	LAL ET AL.	
	Examin r	Art Unit	
	Prema M Mertz	1646	

-- The MAILING DATE f this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7-14,16 and 21-27* is/are pending in the application.

4a) Of the above claim(s) *7,8,16,21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,9-14 and 23-27* is/are rejected. 26-27

7)☒ Claim(s) 25 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants amendment in Paper No. 10 (6/19/03) has been entered. Claims 2, 6, 15 and 17-20 have been canceled in Paper No. 10 (6/19/03). Claims 1, 3-5, 7-14, 16 and 21-27 are pending in the instant application.

Restriction/Election

2. Applicant's election with traverse of Group 13 (original claim 3-5, 9-14 and new claims 23-27) in Paper No.10 (6/19/03) is acknowledged. The traversal is on the ground(s) that the restriction is improper since the examiner has not shown that there is no unity of invention between the various polynucleotides claimed and the various polypeptides encoded by the polynucleotides. Applicant's arguments with respect to including claim 1 drawn to a polypeptide of SEQ ID NO:14 are persuasive and claim 1 will be examined with the polynucleotides claims 3-5, 9-14, 23-27. However, with respect to all the other claimed polynucleotides and polypeptides, Applicants arguments are not found to be persuasive because the PCT rules define a special technical feature as a feature, which defines a contribution over the prior art. The first claimed invention drawn to a polypeptide of SEQ ID NO:14 and polynucleotide encoding such fails to recite such a feature, since a polynucleotide that can hybridize to the polynucleotide of SEQ ID NO:29 (as recited in claim 5 is found in the prior art). Dougherty et al (1992) discloses a polynucleotide encoding human pyrroline-5-carboxylate reductase cDNA that can hybridize to the claimed polynucleotide under the hybridizing conditions recited in claim 5 (see abstract and attached Sequence Comparison "A"). Since the first claimed invention lacks a special technical feature, the other claimed inventions cannot share a special technical feature with the first claimed invention.

The special technical feature of the invention encompassing the polypeptide encoding the polypeptide of SEQ ID NO:14 is the amino acid sequence of SEQ ID NO:14. The other polypeptides (SEQ ID NO:1-8, 10-13, 15) listed do not share the special technical feature (SEQ ID NO:14) because the other polypeptides are structurally and functionally different and examination of all these peptides would place undue examination burden on the Examiner.

The test for propriety of restriction is not whether the inventions are related but rather whether they are distinct and whether it would impose a burden on the examiner to search and examine multiple inventions in a single invention. The different polypeptides and polypeptides are related as different products which are independent and distinct, each from the other, which possess characteristic differences in structure and each has an independent utility, that is distinct for each invention which cannot be exchanged.

Lastly the inventions are distinct because a search of the literature for the polypeptide of SEQ ID NO:14, would not be expected to reveal art for all the other polypeptides, which searches are extensive requiring separate searches, which would be unduly burdensome.

The Groups as delineated in the restriction requirement (Paper No. 8, 5/16/03) are patentably distinct one from the other such that each invention could, by itself, in principle, support its own separate patent (as shown by the arguments put forth in the written restriction requirement).

The requirement is still deemed proper and is therefore made FINAL.

Claims drawn to polynucleotides encoding polypeptides set forth in SEQ ID NO: 1-8, 10-13, 15 and claims 7-8, 16, 21-22 are withdrawn from further consideration by the examiner, 37

CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 10 (6/19/03).

Furthermore, Applicants request rejoinder of the subject matter of method claims 7-8 (see In re Ochiai (37 USPQ2d 1127 (Fed. Cir. 1995)), in which a new, unobvious material is used in a known process. Ochiai determined that a process was free of the prior art if it employed a product which was free of the prior art. However, only if the product claims (polynucleotide and polypeptide) are found allowable, the subject matter of claims 7-8 will be rejoined with the process claims 7-8, if the process claims are of the same scope as the allowable product claims.

Specification

2. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim objections

3. Claim 1 is objected to for the following reason:

Claim 1 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form.

Claim 1 is improperly dependent on claim 3 because clearly, the product of claim 1 as recited can be obtained from natural sources. Therefore, instant claim 1 does not infringe the polynucleotide of claim 3. A proper dependent claim shall not conceivably be infringed by anything which would not also infringe the basic claim. See MPEP § 608.01(n), "Infringement Test" for dependent claims.

Appropriate correction is requested.

Claim Rejections - 35 USC § 112, first paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4a. Claims 1, 3, 5, 9, 11-14, 23-24, 26, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO:29 and equivalent degenerative codon sequences thereof and therefore the written description is not commensurate in scope with the claims drawn to "naturally occurring" polynucleotide variants encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:14 as recited for example in claim 3(b).

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID NO:41, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement, which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Support for allelic variants is provided in the specification on pages 16-17. However, no disclosure, beyond the mere mention of variants is made in the specification. This is insufficient

to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only an isolated nucleic acid molecule comprising a nucleic acid sequence consisting of SEQ ID NO:29 and equivalent degenerative codon sequences thereof, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

Claim 11 recites "comprising at least 60 contiguous nucleotides" and encompasses a genus of nucleic acid molecules comprise only portions of the full-length sequence of SEQ ID NO:29 as well as variants having one or more nucleotide deletions, insertions and/or additions made to SEQ ID NO: 29. The specification and claim do not indicate what are the distinguishing attributes shared by the members of the genus for which the common portion is responsible for functional activity. The specification and claim do not place any limit on the number of nucleotides that may be added to the portions since the claim is not limited to the full-length SEQ ID NO:29. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide a written description as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural and functional attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, nucleic acid molecules comprising at least 60 contiguous nucleotides of SEQ ID NO:29 alone are insufficient

to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus.

4b. Claim 11 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide comprising the nucleotide sequence set forth in SEQ ID NO:29, does not reasonably provide enablement for a polynucleotide comprising at least 60 nucleotides of SEQ ID NO:29 as recited in claim 11. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claimed genus of polynucleotide molecules encompasses variants that do not share activity of the polypeptide, however, the specification does not teach how to make a polynucleotide molecule encoding a polypeptide having an amino acid sequence less than SEQ ID NO:14. The specification only enables a nucleic acid molecule encoding a protein of amino acid sequences set forth in SEQ ID NO:29, and is not enabled for a nucleic acid molecule of nucleotide sequence anything less than what is disclosed in SEQ ID NO:29.

The issue in the instant case is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. The recitation of "at least 60 contiguous nucleotides..." in claim 11, is not a sufficient structural limitation and broadly encompasses any nucleic acid molecule comprising 60 contiguous nucleotide sequences recited in the claims. Because of the presence of the term "comprising" in claim 11, the claim encompasses over 5×10^{100} embodiments.

Furthermore, Applicants have not taught how to make the instant nucleic acid molecules with the stretch of 60 contiguous nucleotides as recited in claim 11. The instant claims are not limited to naturally-occurring compounds and the instant specification does not provide a description of a repeatable process of producing a nucleic acid molecule as claimed.

4c. Claim 1, 3, 9, 11, 12-14, 26-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide encoding a polypeptide comprising the amino acid sequence set forth in SEQ ID NO:14, does not reasonably provide enablement for an isolated polynucleotide encoding a polypeptide comprising an amino acid sequence at least 90 % amino acid sequence identity to SEQ ID NO:14. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 3, for example, is overly broad in the recitation of "at least 90% identical to an amino acid sequence" since no guidance is provided as to which of the myriad of polynucleotide species encoding polypeptide species encompassed by the claim will retain the desired characteristics. Applicants disclose that variants of the polynucleotide can be generated by conservative or nonconservative changes, allelic, splice species or polymorphic variants, without disclosing any actual or prophetic examples on expected performance parameters of any of the possible muteins of SEQ ID NO:14 (page 15, lines 3-22). There is no guidance provided in the specification as to how one of ordinary skill in the art would generate a nucleic acid sequence encoding a polypeptide other than that exemplified in the specification. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered

when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claim rejections-35 USC § 112, second paragraph

5. Claims 1, 3-5, 9-10, 12-14, 23-24, 26-27 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3-5, 9-10, 12-14, are vague and indefinite because they recite non-elected subject matter. Appropriate correction is requested.

Claims 3, 9, 23, 24, 26 are indefinite in the recitation of the term "naturally occurring". It is unclear whether this term imposes a required limitation on the claim, such that it only encompasses, for example, nucleic acid molecules amplified from cDNA or all nucleic acid molecules that encode the polypeptide. Therefore, the metes and bounds of the claim are unclear.

Claim 5 recites "hybridizes" and recites the hybridization conditions which renders the claim vague and indefinite because it is not the hybridization conditions but the wash conditions that are important in determining whether the matches between the polynucleotide molecules are perfect or imperfect. Higher the stringency of the washing conditions, more perfect matches are required, however, if the stringency of washing is low, then less perfect matches are required.

Claims 3 and 23 are rejected as vague and indefinite for reciting "immunogenic fragment". It is unclear what the metes and bounds of this term are. It is suggested that the claim be amended to incorporate the size of the specific immunogenic fragments supported by the specification.

Claims 24, 26-27 are rejected as vague and indefinite insofar as they depend on the above rejected claims for their limitations.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 5, 23 are rejected under 35 U.S.C. 102(a) as being anticipated by Dougherty et al (1992).

The reference discloses a cDNA encoding a pyroline-5-carboxylase reductase (see abstract, page 871; pages 872, Figure 3, column 2). A copy of the comparison of SEQ ID NO:14 of the polypeptide of the instant invention and the polypeptide disclosed in the reference is enclosed at the end of this action (SEQUENCE COMPARISON A). Therefore, an

immunogenic fragment of the polypeptide of the reference, would potentially be any six amino acids. Furthermore, according the limitations of claim 5 in the instant application, the polynucleotide of the reference would potentially be capable of hybridizing to the polynucleotide of SEQ ID NO:29 described in the instant application. Therefore, the cDNA and polypeptide disclosed in the reference meets the limitations of claims 1, 3, 5, 23.

Conclusion

No claim is allowable.

Claim 25 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (703) 308-4229. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564.

Official papers filed by fax should be directed to (703) 305-3014 or (703 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 746-5300.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Prema Mertz

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
July 17, 2003